

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representation of  
The original documents submitted by the applicant.

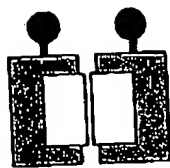
Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

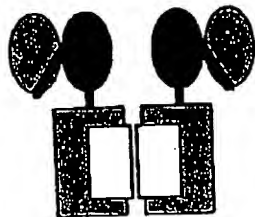
**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

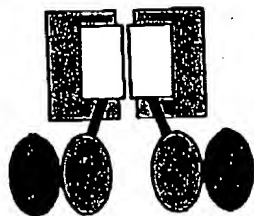
Figure 1



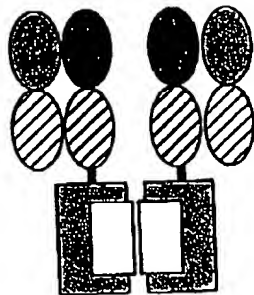
(A) Small ligand-Caspase Hetero-tetramer (after N-terminal processing)



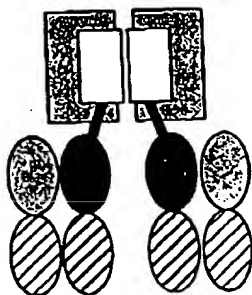
(B) Single-chain Fv (VL-VH format)-Caspase Hetero-tetramer



(C) Caspase Hetero-tetramer-Single-chain Fv (VL-VH format)



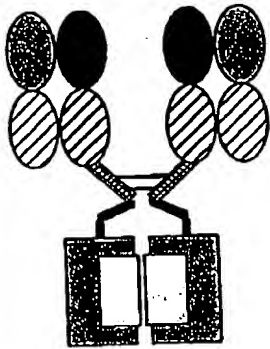
(D) Fab-(Heavy chain fusion)-Caspase Hetero-tetramer



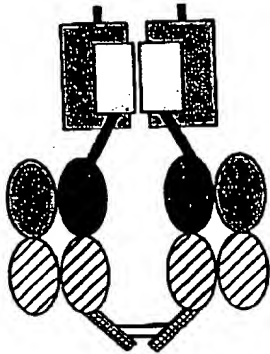
(E) Caspase Hetero-tetramer Fab-(Heavy chain fusion)

2/20

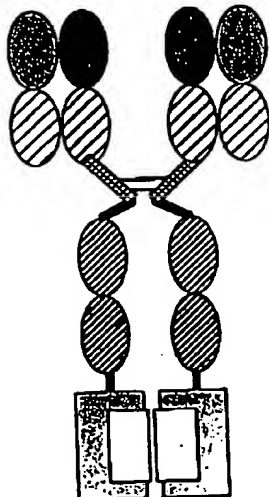
Figure 1 (cont)



(F) F(ab')<sub>2</sub>-Caspase heterotetramer  
Heavy chain fusion

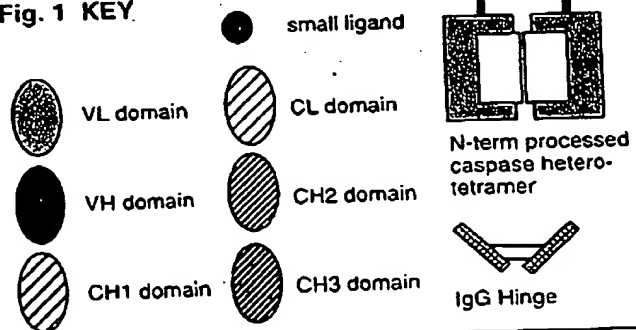


(G) Caspase heterotetramer-F(ab')<sub>2</sub>  
Heavy chain fusion



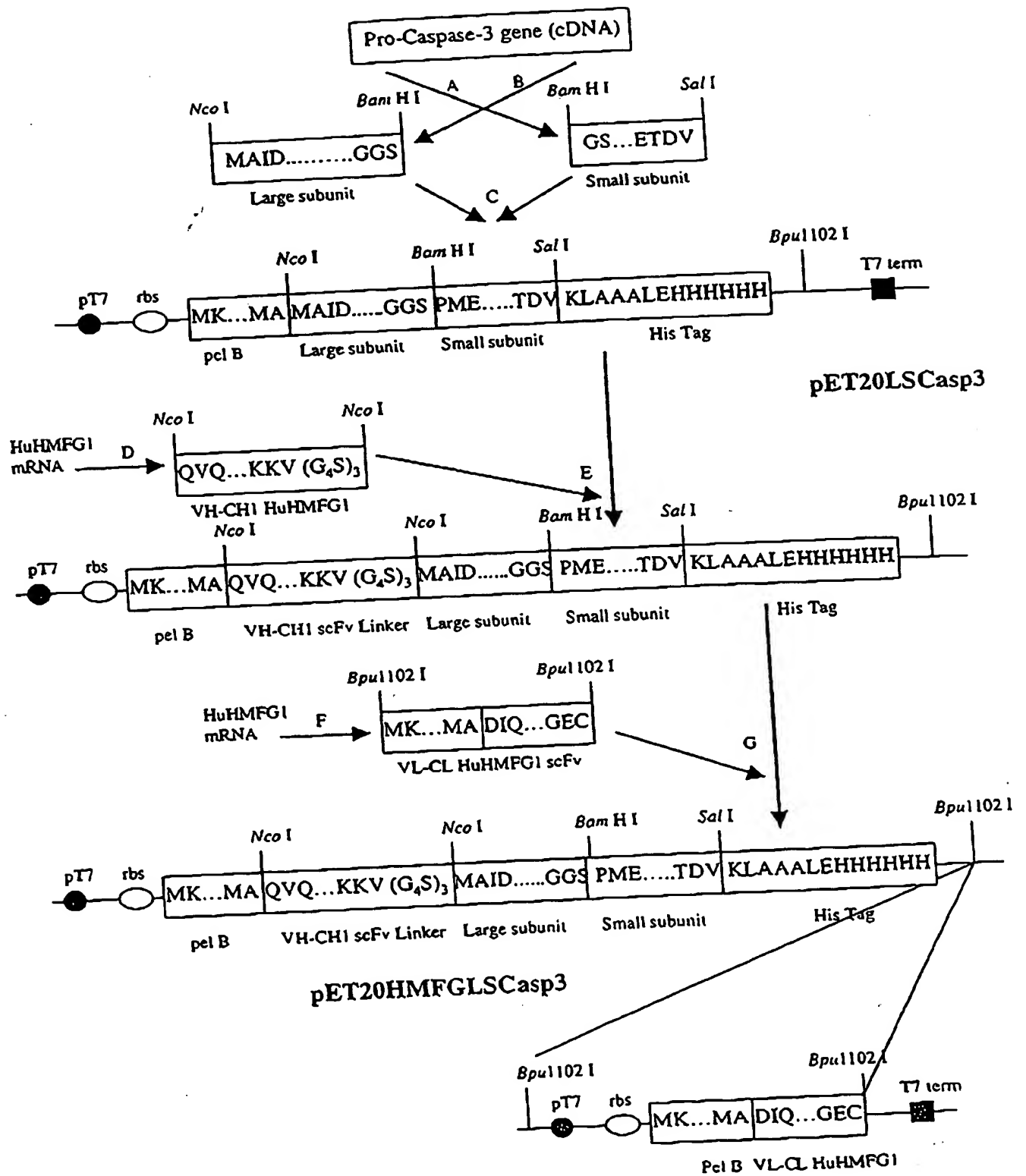
(H) IgG-Caspase heterotetramer

Fig. 1 KEY



3/20

Figure 2



4/20

Figure 3

1  
ATGAAATACCTATTGCCTACGGCAGCCGCTGGATTGTTATTACTCGCGGCCCCAGCCGGG  
M K Y L L P T A A A G L L L L A A Q P A

60  
61  
ATCGCCAGGTGCAGCTGGTGCAGTCTGGGGCAGAGGTGAAAAAGCCTGGGGCCTCAGTG  
M A Q V Q L V Q S G A E V K K P G A S V

120  
121  
AAGGTGTCCTGCAAGGCTTCTGGCTACACCTTCAGTGCCTACTGGATAGAGTGGGTGCGC  
K V S C K A S G Y T F S A Y W I E W V R

180  
181  
CAGGCTCCAGGAAAGGGCCTCGAGTGGGTCTGGAGAGATTTTACCTGGAAGTAATAATTCT  
Q A P G K G L E W V G E I L P G S N N S

240  
241  
AGATACAATGAGAAGTTCAAGGGCCGAGTGACAGTCACTAGAGACACATCCACAAACACA  
R Y N E K F K G R V T V T R D T S T N T

300  
301  
GCCTACATGGAGCTCAGCAGCCTGAGGTCTGAGGACACAGCCGTCTATTACTGTGCAAGA  
A Y M E L S S L R S E D T A V Y Y C A R

360  
361  
TCCTACGACTTTGCCTGGTTTGCTTACTGGGGCCAAGGGACTCTGGTCACAGTCTCCTCA  
S Y D F A W F A Y W G Q G T L V T V S S

420

5/20

Figure 3 (cont)

421  
GCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGG  
A S T K G P S V F P L A P S S K S T S G

481  
GGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCCG  
G T A A L G C L V K D Y F P E P V T V S

541  
TGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCA  
W N S G A L T S G V H T F P A V L Q S S

601  
GGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACC  
G L Y S L S S V V T V P S S S L G T Q T

661  
TACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGGTGGGA  
Y I C N V N H K P S N T K V D K K V G G

721  
GGCGGTTTCAGGCGGAGGTGGCTCTGGTGGAGGCGGTTTCGATGCGATCGATACAGACAGT  
G G S G G G S G G G S M A I D T D S

1261  
GGTGTGATGATGACATGGCGTGTCTATAAAATACCAGTGGATGCCGACTTCTTGATGCA  
G V D D D M A C H K I P V D A D F L Y A

1321  
TACTCCACAGCACCTGGTTATTATTCTTGGCGAAATTCAAAGGATGGCTCCTGGTTCATC  
Y S T A P G Y Y S W R N S K D G S W F I

6/20

Figure 3 (cont)

1381 1440  
CAGTCGCTTTGTGCCATGCTGAAACAGTATGCCGACAAGCTTGAATTTATGCACATTCTT  
Q S L C A M L K Q Y A D K L E F M H I L

1441 1500  
ACCCGGGTTAACCGAAAGGTGGCAACAGAATTTGAGTCCTTTTCCTTTGACGCTACTTTT  
T R V N R K V A T E F E S F S F D A T F

1501 1560  
CATGCAAAGAAACAGATTCCATGTATTGTTTCCATGCTCACAAAAGAACTCTATTTTAT  
H A K K Q I P C I V S M L T K E L Y F Y

~~SECRET~~

1561 1620  
CACGATGAAGTTGATGGTGGATCGCCGATGGAGAACACTGAAAACACTACGTGGATTCAAAA  
H D E V D G G S P M E N T E N S V D S K

781 840  
TCCATTAAAAATTTGGAACCAAAGATCATAATGGAAGCGAATCAATGGACTCTGGAATA  
S I K N L E P K I I H G S E S M D S G I

841 900  
TCCCTGGACAACAGTTATAAAATGGATTATCCTGAGATGGGTTTATGTATAATAATTAAT  
S L D N S Y K M D Y P E M G L C I I I N

901 960  
AATAAGAATTTTCATAAAAGCACTGGAATGACATCTCGGTCTGGTACAGATGTCGATGCA  
N K N F H K S T G M T S R S G T D V D A

961 1020  
GCAAACCTCAGGGAAACATTTCAGAACTTGAAATATGAAGTCAGGAATAAAAATGATCTT  
A N L R E T F R N L K Y E V R N K N D L

7/20

Figure 3 (cont)

1021 1080  
ACACGTGAAGAAATTGTGGAATTGATGCGTGATGTTTCTAAAGAAGATCACAGCAAAGG  
T R E E I V E L M R D V S K E D H S K R

1081 1140  
AGCAGTTTTGTTTGTGTGCTTCTGAGCCATGGTGAAGAAGGAATAATTTTGGAAACAAAT  
S S F V C V L L S H G E E G I I F G T N

1141 1200  
GGACCTGTTGACCTGAAAAAATAACAACTTTTTTCAGAGGGGATCGTTGTAGAAGTCTA  
G P V D L K K I T N F F R G D R C R S L

1201 1260  
ACTGGAAAACCCAACTTTTCATTATTCAGGCCTGCCGTGGTACAGAACTGGACTGTGGC  
T G K P K L F I I Q A C R G T E L D C G

521.1

1261 1320  
ATTGAGACACAGGTCCACAAGCTTGCGGCCGCACTCGAGCACCACCACCACCACCACTGA  
I E T D V D K L A A A L E H H H H H \*

521.102.1

1321 1380  
GATCCGGCTGCTAACAAAGCCCGAAAGGGCTGAGTTGGCTGCTGCCACCGGTGAGCGAAA

1381 1440  
TTAATACGACTCACTATAGGGAGACCACAACGGTTTCCCTCTAGAAATAATTTTGTTTAA



8/20

Figure 3 (cont)

1441 1500  
CTTTAAGAAGGAGATATACATATGAAATACCTATTGCCTACGGCAGCCGCTGGATTGTTA  
M K Y L L P T A A A G L L

1501 1560  
TTACTCGCGGCCAGCCGGCAATGGCCGACATCCAGATGACCCAGAGCCCAAGCAGCCTG  
L L A A Q P A M A D I Q M T Q S P S S L

1561 1620  
AGCGCCAGCGTGGGTGACAGAGTGACCATCACCTGTAAGTCCAGTCAGAGCCTTTTATAT  
S A S V G D R V T I T C K S S Q S L L Y

1621 1680  
AGTAGCAATCAAAAGATCTACTTGGCCTGGTACCAGCAGAAGCCAGGTAAGGCTCCAAAG  
S S N Q K I Y L A W Y Q Q K P G K A P K

1681 1740  
CTGCTGATCTACTGGGCATCCACTAGGGAATCTGGTGTGCCAAGCAGATTCAGCGGTAGC  
L L I Y W A S T R E S G V P S R F S G S

1741 1800  
GGTAGCGGTACCGACTTCACCTTCACCATCAGCAGCCTCCAGCCAGAGGACATCGCCACC  
G S G T D F T F T I S S L Q P E D I A T

1801 1860  
TACTACTGCCAGCAATATTATAGATATCCTCGGACGTTCCGGCCAAGGGACCAAGGTGGAA  
Y Y C Q Q Y Y R Y P R T F G Q G T K V E

1861 1920  
ATCAAACGAACTGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTG  
I K R T V A A P S V F I F P P S D E Q L

9/20

Figure 3 (cont)

1921 1980  
AAATCTGGAAGTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAA  
K S G T A S V V C L L N N F Y P R E A K

1981 2040  
GTACAGTGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAG  
V Q W K V D N A L Q S G N S Q E S V T E

2041 2100  
CAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAAGCAGAC  
Q D S K D S T Y S L S S T L T L S K A D

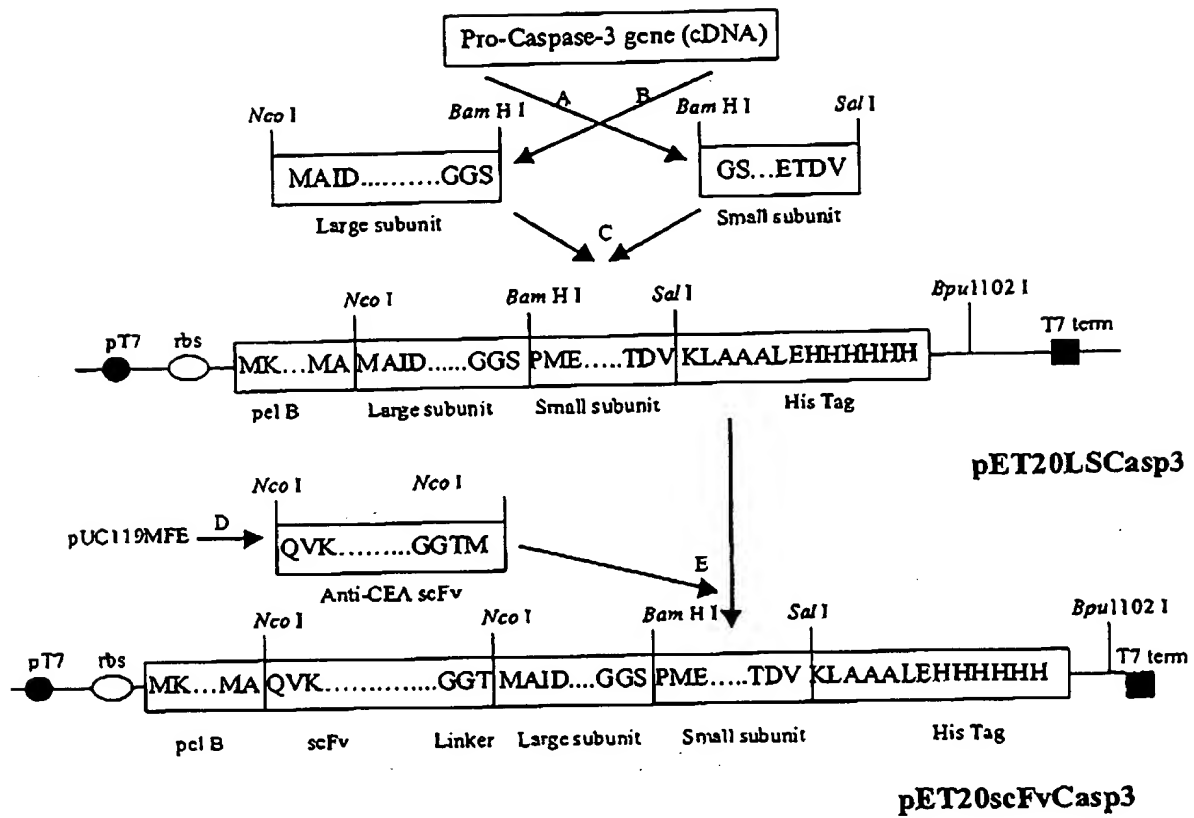
2101 2160  
TACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTC  
Y E K H K V Y A C E V T H Q G L S S P V

2161 2206  
ACAAAGAGCTTCAACAGGGGAGAGTGTTAGTAGCAATGGGGTGGC  
T K S F N R G E C \* \*

BBB102 I

10/20

Figure 4



## Figure 5

10 20 30 40 50 60  
CCATGGGGCAGGTGAAACTGCAGCAGTCTGGGGCAGAACTTGTGAGGTCAGGGACCTCAG  
GGTACCCCGTCCACTTTGACGTCGTCAGACCCCGTCTTGAACACTCCAGTCCCTGGAGTC  
M G Q V K L Q Q S G A E L V R S G T S

70 80 90 100 110 120  
TCAAGTTGTCCTGCACAGCTTCTGGCTTCAACATTAAAGACTCCTATATGCACTGGTTGA  
AGTTCAACAGGACGTGTCGAAGACCGAAGTTGTAATTTCTGAGGATATACGTGACCAACT  
V K L S C T A S G F N I K D S Y M H W L

130 140 150 160 170 180  
GGCAGGGGCCTGAACAGGGCCTGGAGTGGATTGGATGGATTGATCCTGAGAATGGTGATA  
CCGTCCCCGGACTTGTCCCGGACCTCACCTAACCTACCTAACTAGGACTCTTACCACTAT  
R Q G P E Q G L E W I G W I D P E N G D

190 200 210 220 230 240  
CTGAATATGCCCCGAAGTTCCAGGGCAAGGCCACTTTTACTACAGACACATCCTCCAACA  
GACTTATACGGGGCTTCAAGGTCCCGTTCCGGTGAAAATGATGTCTGTGTAGGAGGTTGT  
T E Y A P K F Q G K A T F T T D T S S N

250 260 270 280 290 300  
CAGCCTACCTGCAGCTCAGCAGCCTGACATCTGAGGACACTGCCGTCTATTATTGTAATG  
GTCGGATGGACGTCGAGTCGTCGGACTGTAGACTCCTGTGACGGCAGATAATAACATTAC  
T A Y L Q L S S L T S E D T A V Y Y C N

## Figure 5 (cont)

310 320 330 340 350 360  
AGGGGACTCCGACTGGGCCGTACTACTTTGACTACTGGGGCCAAGGGACCACGGTCACCG  
TCCCCTGAGGCTGACCCGGCATGATGAACTGATGACCCCGGTTCCCTGGTGCCAGTGGC  
E G T P T G P Y Y F D Y W G Q G T T V T

370 380 390 400 410 420  
TCTCCTCAGGTGGAGGCGGTTCAAGCGGAGGTGGCTCTGGCGGTGGCGGATCAGAAAATG  
AGAGGAGTCCACCTCCGCCAAGTCCGCCTCCACCGAGACCGCCACCGCCTAGTCTTTTAC  
V S S G G G S G G G S G G G S E N

430 440 450 460 470 480  
TGCTCACCCAGTCTCCAGCAATCATGTCTGCATCTCCAGGGGAGAAGGTCACCATAACCT  
ACGAGTGGGTCAGAGGTCGTTAGTACAGACGTAGAGGTCCCCTCTTCCAGTGGTATTGGA  
V L T Q S P A I M S A S P G E K V T I T

490 500 510 520 530 540  
GCAGTGCCAGCTCAAGTGTAAGTTACATGCACTGGTTCCAGCAGAAGCCAGGCACTTCTC  
CGTCACGGTCGAGTTCACATTCAATGTACGTGACCAAGGTCGTCTTCGGTCCGTGAAGAG  
C S A S S S V S Y M H W F Q Q K P G T S

550 560 570 580 590 600  
CCAAACTCTGGATTTATAGCACATCCAACCTGGCTTCTGGAGTCCCTGCTCGCTTCAGTG  
GGTTTGAGACCTAAATATCGTGTAGGTTGGACCGAAGACCTCAGGGACGAGCGAAGTCAC  
P K L W I Y S T S N L A S G V P A R F S

## Figure 5 (cont)

610            620            630            640            650            660  
GCAGTGGATCTGGGACCTCTTACTCTCTCACAATCAGCCGAATGGAGGCTGAAGATGCTG  
CGTCACCTAGACCCTGGAGAATGAGAGAGTGTTAGTCGGCTTACCTCCGACTTCTACGAC  
G S G S G T S Y S L T I S R M E A E D A

670            680            690            700            710            720  
CCACTTATTACTGCCAGCAAAGGAGTAGTTACCCACTCACGTTCCGGTGCTGGCACCAAGC  
GGTGAATAATGACGGTCGTTTTCCTCATCAATGGGTGAGTGCAAGCCACGACCGTGGTTCCG  
A T Y Y C Q Q R S S Y P L T F G A G T K

730            740            750            760            770            780  
TGGAGCTGCAACCGGGAGGTTCTGGAGGAACCATGGCGATCGATACAGACAGTGGTGTTG  
ACCTCGACGTTGGCCCTCCAAGACCTCCTTGGTACCGCTAGCTATGTCTGTCACCACAAC  
L E L Q P G G S G G T M A I D T D S G V

790            800            810            820            830            840  
ATGATGACATGGCGTGTCATAAAATACCAGTGGATGCCGACTTCTTGTATGCATACTCCA  
TACTACTGTACCGCACAGTATTTTATGGTCACCTACGGCTGAAGAACATACGTATGAGGT  
D D D M A C H K I P V D A D F L Y A Y S

850            860            870            880            890            900  
CAGCACCTGGTTATTATTCTTGGCGAAATTCAAAGGATGGCTCCTGGTTCATCCAGTCGC  
GTCGTGGACCAATAATAAGAACCGCTTTAAGTTTCCTACCGAGGACCAAGTAGGTCAGCG  
T A P G Y Y S W R N S K D G S W F I Q S

## Figure 5 (cont)

910 920 930 940 950 960  
TTTGTGCCATGCTGAAACAGTATGCCGACAAGCTTGAATTTATGCACATTCTTACCCGGG  
AAACACGGTACGACTTTGTCATACGGCTGTTTGAAGTAAATACGTGTAAGAATGGGCCC  
L C A M L K Q Y A D K L E F M H I L T R

970 980 990 1000 1010 1020  
TTAACCGAAAGGTGGCAACAGAATTTGAGTCCTTTTCCTTTGACGCTACTTTTCATGCAA  
AATTGGCTTTCCACCGTTGTCTTAAACTCAGGAAAAGGAACTGCGATGAAAAGTACGTT  
V N R K V A T E F E S F S F D A T F H A

1030 1040 1050 1060 1070 1080  
AGAAACAGATTCCATGTATTGTTTCCATGCTCACAAAAGAACTCTATTTTTATCACGATG  
TCTTTGTCTAAGGTACATAACAAAGGTACGAGTGTTTTCTTGAGATAAAAATAGTGCTAC  
K K Q I P C I V S M L T K E L Y F Y H D

1090 1100 1110 1120 1130 1140  
AAGTTGATGGTGGATCCCCGATGGAGAACACTGAAAACACTGCGATTCAAATCCATTA  
TTCAACTACCACCTAGGGGCTACCTCTTGTGACTTTTGATGCACCTAAGTTTTAGGTAAT  
E V D G G S P M E N T E N Y V D S K S I

1150 1160 1170 1180 1190 1200  
AAAATTTGGAACCAAAGATCATACATGGAAGCGAATCAATGGACTCTGGAATATCCCTGG  
TTTTAAACCTTGGTTTCTAGTATGTACCTTCGCTTAGTTACCTGAGACCTTATAGGGACC  
K N L E P K I I H G S E S M D S G I S L

## Figure 5 (cont)

1210 1220 1230 1240 1250 1260  
ACAACAGTTATAAAATGGATTATCCTGAGATGGGTTTATGTATAATAATTAATAATAAGA  
TGTTGTCAATATTTTACCTAATAGGACTCTACCCAAATACATATTATTAATTATTATTCT  
D N S Y K M D Y P E M G L C I I I N N K

1270 1280 1290 1300 1310 1320  
ATTTTCATAAAAGCACTGGAATGACATCTCGGTCTGGTACAGATGTCGATGCAGCAAACC  
TAAAAGTATTTTCGTGACCTTACTGTAGAGCCAGACCATGTCTACAGCTACGTCGTTTGG  
N F H K S T G M T S R S G T D V D A A N

1330 1340 1350 1360 1370 1380  
TCAGGGAAACATTTCAGAACTTGAAATATGAAGTCAGGAATAAAAATGATCTTACACGTG  
AGTCCCTTTGTAAGTCTTTGAACTTTATACTTCAGTCCTTATTTTTACTAGAATGTGCAC  
L R E T F R N L K Y E V R N K N D L T R

1390 1400 1410 1420 1430 1440  
AAGAAATTGTGGAATTGATGCGTGATGTTTCTAAAGAAGATCACAGCAAAGGAGCAGTT  
TTCTTTAACACCTTAACTACGCACTACAAAGATTTCTTCTAGTGTCGTTTTCTCGTCAA  
E E I V E L M R D V S K E D H S K R S S

1450 1460 1470 1480 1490 1500  
TTGTTTGTGTGCTTCTGAGCCATGGTGAAGAAGGAATAATTTTTGGAACAAATGGACCTG  
AACAAACACACGAAGACTCGGTACCACTTCTTCCTTATTAAAAACCTTGTTTACCTGGAC  
F V C V L L S H G E E G I I F G T N G P



1510	1520	1530	1540	1550	1560
TTGACCTGAAAAAATAACAACTTTTT	CAGAGGGGATCGTTGTAGAAAGTCTAACTGGAA				
AACTGGACTTTTTTTATTGTTTGAAAAAGTCTCCCCTAGCAACATCTTCAGATTGACCTT					
V	D	L	K	K	I
					T
					N
					F
					F
					R
					G
					D
					R
					C
					R
					S
					L
					T
					G

1570	1580	1590	1600	1610	1620														
AACCCAACTTTTCATTATTCAGGCCTGCCGTGGTACAGAACTGGACTGTGGCATTGAGA																			
TTGGGTTTGAAAAGTAATAAGTCCGGACGGCACCATGTCTTGACCTGACACCGTAACTCT																			
K	P	K	L	F	I	I	Q	A	C	R	G	T	E	L	D	C	G	I	E

[illegible]

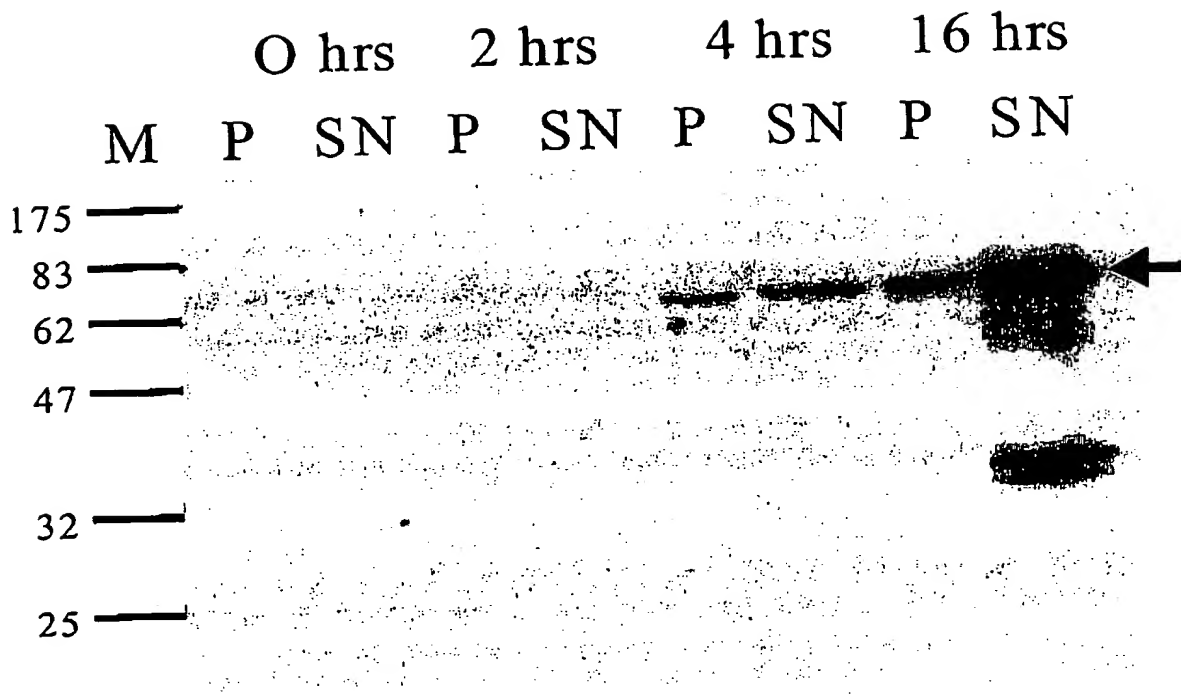
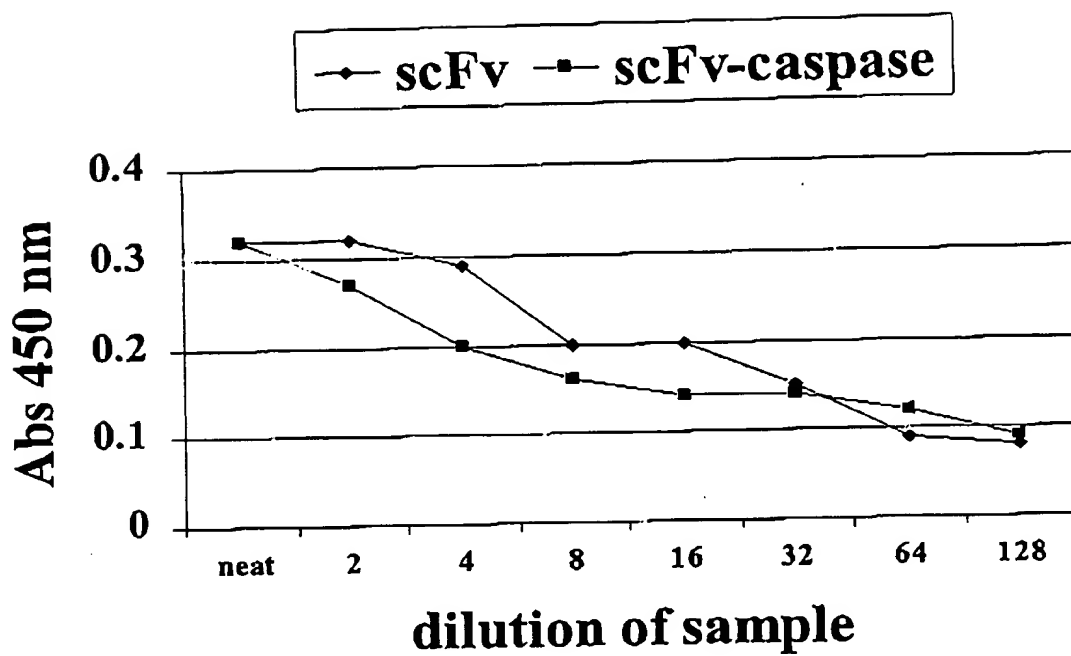
**Figure 6**

Figure 7



**Figure 8**

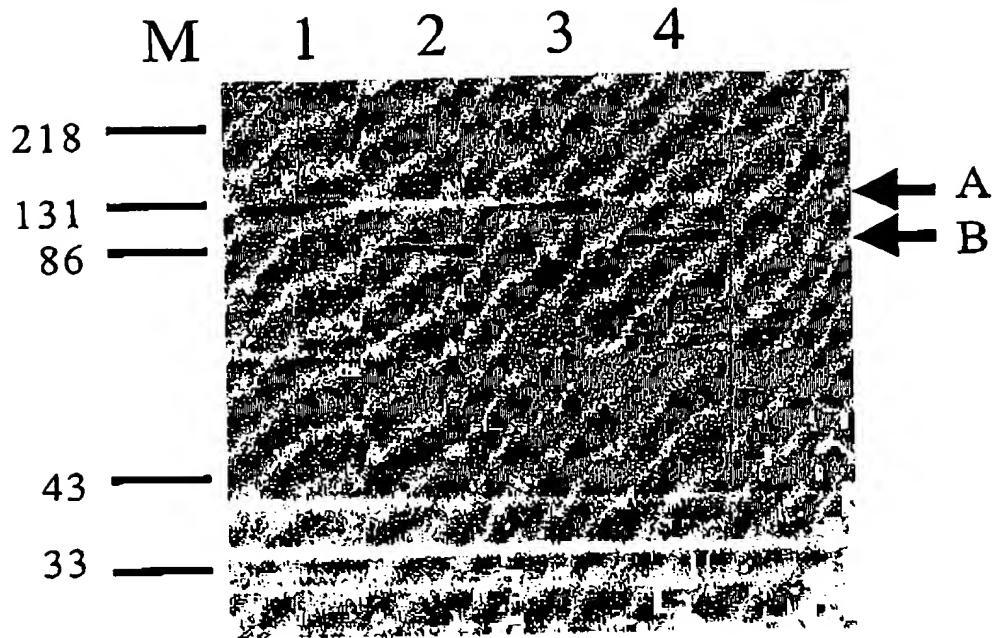


Figure 9

